

**Editorial**

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Epidemiology of Complexity in General Medicine

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Received Date: July 15, 2026**Published Date: July 21, 2026**

Keywords: Complexity; Biopsychosocial; Methodology; Epidemiology; General practitioner: Public Health

Editorial

Epidemiology is a procedure for finding things, asking questions, and obtaining answers that generate further questions; in other words, a method [1]. Classical epidemiology, or epidemiology in simple systems, seeks single or primary causes. For example, does the patient have strep throat? Or, which drug is most effective in treating angina pectoris? The human body is viewed as a “machine” with parts that are repaired in isolation. It is based on the cause-and-effect model (agent-host-environment). A direct cause-and-effect relationship is sought. It is predictable and works well for classic infectious diseases with known and direct transmission mechanisms, where specific risks can be identified. It assumes linearity (one cause produces a proportional effect), closed or near-equilibrium systems, and high long-term predictability. However, causality becomes difficult to establish when multiple factors interact [2-4].

And therein lies the problem: in health/disease, systems are complex. Complexity is the study of adaptive systems, and its key concepts are: self-organization, adaptation, perturbations bordering on chaos, the unpredictability of the effects of small changes in initial conditions, and the existence of simplicity at some

levels while chaos exists at others. The concept and application of epidemiology can vary significantly when applied from simple to complex systems. The transition from simple to complex systems involves a paradigm shift: from a reductionist, linear, and cause-and-effect-centered approach to a holistic, nonlinear, and network-based one, centered on dynamic behavior [5].

Therefore, how does an epidemiology of complexity differ from the traditional approach? In complex systems, the focus is on the relationships between their parts, rather than on the parts themselves; it seeks to understand the interaction mechanisms that generate disease patterns [3]. The human body is composed of multiple interacting and self-regulating physiological systems, including biochemical and neuroendocrine feedback loops; An individual's behavior is determined partly by an internal set of rules based on past experiences and partly by unique, adaptive responses to new stimuli from the environment. The network of relationships in which individuals operate contains many different factors that determine their beliefs, expectations, and behavior. Furthermore, individuals and their immediate social relationships are more deeply embedded in broader social, political, and cultural systems that can influence outcomes in entirely new and

unpredictable ways. To all this, we must add that these interacting systems are dynamic and fluid, and that a small change in one part of this network of interacting systems can trigger a much larger change elsewhere through amplification effects. By intervening in one complex system, we often generate effects in other areas. This is becoming increasingly evident in our efforts to address the large-scale health problems that our own actions have created [6,7]. In other words, biological and social systems are inherently complex, so it is not surprising that few or no human health problems can be said to have a single “cause” or “cure” [8].

The epidemiology of complexity maintains a systems approach. It conceptualizes health as the result of a multitude of interdependent elements (adaptive agents) that interact nonlinearly, where the whole is more than the sum of its parts. Its characteristics include high sensitivity to initial conditions, nonlinear behavior, constant feedback, and emergent properties (patterns that cannot be predicted by studying the components separately). This approach is necessary to address chronic diseases (obesity, diabetes, etc.), pandemics (COVID-19), social interactions (contact networks), and public health decision-making.

Its tools are:

- 1) Quantitative methods using mathematical computational modeling (systems dynamics) to simulate complex scenarios and predict non-obvious interventions [9].

And

- 2) qualitative: stemming from its positivist origins, systems thinking tends to reduce complexity by modeling it in mathematical terms (interdependencies between system components), while being unable to fully capture and make sense of social, relational, and political dynamics, such as disagreement over the framing of problems and solutions or conflicts between stakeholders [10]. The classical approach to complexity theory directs researchers to identify the rules governing these behaviors, attributing them to the agent (local rules) or to an environmental pattern (attractors). In this classical interpretation of complexity theory, established research methods include agent-based modeling, simulation, and network analysis, where a theory of local rules is integrated into a mathematical model that is then tested against reality. However, these approaches have had limited success in the healthcare sector, and low model implementation rates are often attributed to a lack of adequate data for their development; Recent applications of complexity theory to the healthcare sector have extended to more qualitative methods, such as ethnography, case studies, case and comparative analyses, time series studies, and social surveys [11].

Despite the increased interest in complexity theory in healthcare over the past 30 years [12], the theorizing and empirical examination of complexity remain suboptimal in health services research [13]. There are very few examples of the use of complexity theory in epidemiology—the main ones to date relate to communicable diseases—but there are many examples of epidemiological problems for which complexity theory is relevant, particularly in general practice/family medicine/community

medicine.

Different types of problems require different types of knowledge. The general practitioner, in contrast to hospital specialists, is more frequently engaged in decision-making within complex and chaotic systems, where quantitative data, evidence-based medicine, and clinical protocols or guidelines are insufficient. There are no truly simple, complex, or chaotic problems; rather, it depends on the level of depth of the problem's study: all problems are inherently highly complex, and classifying them otherwise is a matter of convention, based on where we arbitrarily stop our inquiry [14].

At this level of medical practice, the distinction between classical epidemiology and the epidemiology of complexity is key because its approach transcends the traditional biomedical model, analysing the health-disease process as a nonlinear and interconnected system influenced by biological, social, environmental, and behavioural factors. Here, symptom patterns, disease trajectories, and health outcomes are complex entities characterized by a wide range of clinical manifestations and progression patterns. In primary care, complexity is defined not only by the presence of multiple diseases (multimorbidity), but also by their interaction with the patient's social, familial, and functional context, making linear prediction of outcomes and uncertainty management difficult [15].

In the epidemiology of complex systems in family medicine, general practice, and community medicine, health is understood as an emergent phenomenon of multiple interconnected factors [2]. This is especially relevant in the management of multimorbidity: A patient with diabetes, hypertension, and depression is not simply the sum of three clinical guidelines. Treating one condition can worsen another (negative feedback). In complex or chaotic patients (What is the best treatment for a patient experiencing a crisis of intoxication due to excessive alcohol consumption, with angina, depression, cluster headaches, who is a smoker, has legal, economic, and family problems, is religious, has a history of non-compliance, is a frequent consultant, exhibits occasionally hostile behavior, and lives in an isolated rural area?), in uncertain environments where the system has “memory” (the patient's biography) and two patients with the same illness can respond in entirely different ways due to their unique circumstances, as well as considering the crucial influence of social factors (family support network, economic situation, context), the epidemiology of complexity is indispensable.

Biopsychosocial causality emphasizes the importance of the transformative mutual influence of the different interacting causal factors and points out the irrelevance of considering a single determining condition. Cause and effect constantly shift; from the psychosocial to the biological realm, and vice versa. The epidemiological cause-and-effect relationship is a process of displacement or transaction from incomplete material to more complete material. from manifest to latent material. Biopsychosocial causes give rise to scenarios that behave like the plots of television series: the characters, interconnected directly or tangentially, find themselves embroiled in a new mess before they can get out of the previous one. This means that there are several

plots running simultaneously (at least two or three), where various causal stories intertwine, and all of them present moments of knots, entanglements, tangles, disorder, confusion, and confusion, which partially overlap for each character, without a final resolution [16,17].

In summary, in complex systems, epidemiological attention focuses on the relationships between their parts, rather than on the parts themselves. From a methodological and theoretical perspective, the epidemiology of complexity requires a holistic, ecological, contextual, and transdisciplinary approach. The most appropriate epidemiological methods for addressing the complexity of general medicine and public health include mathematical approaches, but also qualitative approaches to fully capture and make sense of social, relational, and political dynamics. However, it may be necessary to develop new epidemiological methods better suited to addressing the complexity of public health. These new methods will likely resemble complex observational research, such as evolutionary biology and cosmology, less a randomized controlled trial and more akin to such research.

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